Remarks

Regarding amendments in the Claims:

The amendment to allowed claim 3 does not change the scope of the claim. The terms "genetic characteristic gene" and "trait-causing polymorphism" are equivalent. The terms "genetic characteristic" and "trait" are equivalent. (See definitions p. 11 lines 7-17.) The amendment is simply being made so that the usage of the terms "gene" and "polymorphism" in the claims is closer to the terms' usual usage. The term "gene" in act e) has been changed to "trait-causing polymorphism", because the applicants neglected to change this term in the previous amendment/response.

Applicants respectfully thank the Examiner for his comments and suggestions in the previous Office Action.

Regarding point 2. A) and claim 102. Claim 102 has been amended. The applicants respectfully request that the Examiner reconsider amended claim 102. The applicants respectfully submit that the amended claim is now in a form that allows the means in the claim to be construed in terms of specific apparatus components. For example, a High-Density DNA array as described in endnote VIII of the application (Accessing Genetic Information with High-Density DNA Arrays, Mark Chee, et al. Science, vol 274, Oct. 25, 1996, pp. 610 – 614.) is a nonlimiting example. In such an array, the a) means of the claim is essentially an array of complementary oligonucleotides (see p. 610); these oligonucleotides are arrayed on a chip (see explanation accompanying Fig. 1A p. 611). And the b) means is essentially one of two dyes, flourescein or phycoerythrin (see p. 611 bottom first column) and a high-resolution confocal scanner that uses a laser (see p. 612 bottom second column and endnote 21 of the paper). Another similar nonlimiting example is the "gene chips" described in endnote IX of the application (Large Scale Identification, Mapping, and Genotyping of Single-Nucleotide Polymorphisms in the Human Genome, Wang, et. al., Science, May 15, 1998, vol 280, pp. 1077-1081). In this example the a) means of the claim is essentially an array of complementary oligonucleotides (see Fig 1 page 1078) and the b) means of the claim is essentially a dye (or stain) and confocal scanner (see third paragraph p. 1078 and endnote 16).

Another nonlimiting example is MALDITOF as described in endnote I (Weighing DNA for Fast Genetic Diagnosis, Science, March 27, 1998, vol. 279, pp. 2044-2045.) In MALDITOF, the a) means of the claim is essentially a group of one or more complementary oligonucleotides that are used as PCR primers in amplification of DNA (see first column 3rd paragraph p. 2045). The amplified DNA is then placed in a matrix which is vaporized by a laser. The b) means of the claim is essentially a mass spectrometer that measures the mass of amplified DNA fragments in the matrix that have been vaporized by the laser (see first column 2nd and 3rd paragraphs p. 2045).

Another nonlimiting example is as described in endnote XI (2) (Genetic analysis of amplified DNA with immobilized sequence- specific oligonucleotide probes, Saiki,et al., Proc Natl Acad Sci USA vol 86, pp.6230-6234). In this example, the a) means of the claim is essentially one or more sequence specific oligonucleotides bound to a nylon membrane (see Abstract p. 6230) and the b) means is essentially a red dye generated by an enzymatic reaction (see 3rd paragraph p. 6230). (Another construction for the a) means of the claim is essentially one or more biotinylated PCR primers (see Abstract, p. 6230).)

Another nonlimiting example is as described in endnote XI (3) (Allele-specific enzymatic amplification of β-globin genomic DNA for diagnosis of sickle cell anemia, Wu, et al., Proc Natl Acad Sci USA vol 86 pp 2757-2760.). In this example, the a) means is essentially one or more allele-specific PCR primers (see abstract and Figure 1 p. 2758) and the b) means is essentially an agarose gel (used for electrophoretic separation) and stain (ethidium bromide) transilluminated by ultraviolet (see p. 2758 1st column, 2nd paragraph). In another version of the invention a) means is essentially one or more allele-specific PCR primers labeled with biotin and/or a flouresecent dye (fluorescein or tetramethyl rhodamine) and the b) means is essentially a flourescent dye detected by flourescence and/or a streptavidin-agarose column (see p. 2758 DISCUSSION and Figure 3 p. 2759).

Another nonlimiting example is as described in endnote XI (4)(Automated DNA diagnostics using an Elisa-based oligonucleotide ligation assay, Nickerson, et al., Proc Natl Acad Sci USA vol 87, pp. 8923-8927.). In this example, the a) means is essentially one or more PCR primers that are biotinylated or labeled with a reporter probe such as Digoxigen and ligated or not ligated covalently by DNA ligase; and the b) means is essentially an ELISA procedure with alkaline phosphatase-conjugated anti-digoxignenin antibodies and a substrate (see Figure 1 and "Ligation Assays" p. 8924 and Abstract p. 8923). (Another construction for the a) means of the claim is essentially one or more PCR primers used for DNA amplification (see Fig. 1 and "DNA Amplification" p. 8924).)

Copies of the published papers described above in the endnotes were included with the applicants' RCE dated 7/18/03. And each of these papers is incorporated by reference into the application.

Another nonlimiting example is as described in endnote X ((1)Schuster, H. et al (1996) Nature Genetics, 13(1) : 98 – 100.). In this example, the a) means is essentially one or more PCR primers, some of which are labeled with flourescent dyes; and the b) means is essentially the flourescent dye(s) which are made to flouresce after electrophoretic separation in a gel. (see p. 100 "**DNA-marker analysis**"). Another nonlimiting example is as described in endnote X ((2)Gyapay, G. et al (1994) Nature Genetics, 7: 246-339.). In this example, the a) means is essentially one or more PCR primers and the b) means is essentially exposure to autoradiographic film after gel separation (see "**Genotyping**" p. 248). Copies of these two papers are enclosed herewith.

The Examiner's attention is directed to p. 20 line 28 to p. 21 line 7 and p.33 line 20 to p. 34 line 18 of the application. The applicants respectfully submit that it is possible that there are other constructions for means a) and/or means b) than those given above, even for individual apparatus described in individual references cited above. And the constructions for the means given in the nonlimiting examples cited above are nonlimiting, even for the particular references and apparatus cited above.
The Examiner states "The specification and noted references refer to a myriad of admittedly well known technologies and devices used therein; there is clearly no indication in the specification as to what actual elements or components are contemplated in the claimed apparatus, let alone why such an apparatus might be patentable" (underlining present in the original). The applicants respectfully submit that actual elements or components contemplated in the claimed apparatus have been indicated. Regarding the issue as to "why such an apparatus might be patentable", the applicants respectfully submit the following explanation. A set of one or more complementary oligonucleotides is essentially the means (or part of the means) of the amended claim 102 and oligonucleotides in the set are essentially complementary to one or more alleles of a group of covering markers that systematically cover a two-dimensional CL-F region. In effect such a group of markers is essentially novel and unobvious; and the set of complementary oligonucleotides is also essentially novel and unobvious. Such a novel and unobvious set of oligonucleotides makes the structure of the apparatus essentially novel and unobvious as well. Thus the structure of the apparatus essentially distinguishes it from prior art, essentially fulfilling the criterion of MPEP 21114 (APPARATUS CLAIMS MUST BE STRUCTURALLY DISTINGUISHABLE FROM PRIOR ART). Applicants respectfully submit that a similar situation is when a general purpose computer is programmed to become a special purpose computer. When a general purpose computer is programmed to carry out an algorithm, *"such programming creates a new machine, because a general purpose computer in effect becomes a special purpose computer once it is programmed to perform particular functions pursuant to instructions from program software"*. The quote is from In re Alappat (31 USPQ2d 1545, 1548; 33 F.3d 1526, 1545).
Again, applicants respectfully thank the Examiner for his comments and suggestions in the previous Office Action.

Regarding point 2 B) and the parenthetical in claims 115, 119 and 145. These claims have been amended and the parentheses have been eliminated. Applicants submit that the scope of these amended claims is not decreased compared to the previous unamended claims.

Regarding point 2 C) and claims 143 and 144. These claims have been amended so that they are now drawn to a method rather than an apparatus.

Regarding point 3 and the provisional double patenting rejection based on claims 2, 3 and 4 in Application No. 10/037, 718. These claims have been canceled by the applicants in a previous response dated March 4, 2004 in order to remove these claims as a basis for the double patenting rejection in the present application.

Some other remarks:

Some claims contain the added limitation: "wherein the essentially one-dimensional panel is based on using increased disequilibrium between a marker and possible trait-causing polymorphism to increase the power of an association-based linkage test, wherein the increased disequilibrium is computed respectively as δ/δ_{max} for $\delta \geq 0$ or δ/δ_{min} for $\delta < 0$, wherein each of the δ values is a value of the coefficient of disequilibrium". It should be noted that the inventor's paper shows that increasing disequilibrium increases the power of an association-based linkage test; and this linkage disequilibrium is computed as above as δ/δ_{max} for $\delta \geq 0$ or δ/δ_{min} for $\delta < 0$. And that linkage disequilibrium varies from zero to 1, and the resulting power varies from zero to a maximum.

It is applicants' position that the added limitation: "wherein the genotype/sample allele frequency data is genotype data or sample allele frequency data or an equivalent thereof" is for the purposes of clarity. The limitation does not decrease the scope of any amended claim, as this limitation is essentially the same as genotype data/sample allele frequency data. That is, for these amended claims, "(2) a combination of genotype data and sample allele frequency data" (see definition p. 21) is essentially an equivalent of genotype data or sample allele frequency data.

In some claims the word "panel" has been substituted for the word "map". This is being done to bring the claims into greater conformity with terminology used in the art. The term "panel" has been added to the specification by amendment for antecedent basis in the claims. The limitation "thousands of covering markers" used in some claims is supported by p. 47 line 5, which describes a genotyping technique. Some claims have been amended so the term "whereby" is substituted for "so that", this has been done for the purposes of clarity and does not change claim scope.

Regarding amendments in the Specification

Amendments to the Background have essentially eliminated some matter previously entered by

amendment after National Phase entry. The Summary section has been eliminated. Other subject matter has been added to the Background by essentially taking subject matter and concepts already in the application from other places (e.g., Background, Description). Similarly an amendment to the "Brief Description of Some Concepts Used By Versions of the Invention" section has essentially used subject matter already in the Description (p. 26 line 23). And extensive additions (four new paragraphs, mathematical expressions, and three Tables) to the Description from the inventor's published paper (which is incorporated by reference into the patent application) have been made. These additions have generally been made from sections or subject matter in the paper referred to in the application. This paper is now freely available to the public online from the publisher, Blackwell, at no cost. The amendment to endnote X has been made because the year was incorrect, the volume, issue and page numbers were, however, correct.

Regarding amendments to the Abstract

A new replacement Abstract has been requested, better reflecting pending claims.

Conclusion

Twenty claims (3 independent, 17 singly dependent) have been favorably examined and allowed in a previous Office Action. These are claims 3-5, 8, 20, 21, 33-35, 38, 50, 51, 78-80, 83, 95 and previously added claims 99-101. Previously allowed claim 3 has been slightly amended.

Extensive amendments to most of previously added claims 102 to 159 have been made. However all of these claims are still based on the new two-dimensional CL-F approach. And 12 new claims 160 to 171 have been added. New arguments and evidence of patentability for amended claim 102 have been respectfully submitted. Extensive amendments to the specification and abstract have been made. An appropriate payment of the fee for the new claims and third month extension is enclosed. For the reasons advanced above, applicants respectfully submit that the application is now in condition for allowance and that action is earnestly solicited. Applicants again express thanks to the Examiner for his observations and comments in the previous Office Actions.

Respectfully submitted,

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